REMARKS

I. Status of the Claims

Reconsideration of the present application is respectfully requested. Claims 1 and 2 are currently amended to recite "naked recombinant nucleic acid" and "within the age of birth to six months." Support for these amendments can be found throughout the specification and in the Examples, specifically in the Example beginning on page 27, and on page 15, lines 13-17, accordingly. Claims 1-2 remain currently pending. No new matter is added by way of these amendments.

II. Rejections under 35 U.S.C. § 102(b)

Claims 1 and 2 stand rejected as anticipated under 35 U.S.C. § 102(b) over Ali et al. (Infect Immun 1982, 38(2):610-19) and Murphy et al. (J Clin Microbiol 1986, 24(2):197-202). According to the Examiner, Ali teaches an infant rat model of administration of attenuated virus for immunization. Additionally, the Examiner states that Murphy discloses immunization using inactivated respiratory syncytial virus vaccine. Since the claims broadly claim methods of immunizing an infant against any antigen and by any route of administration, the Examiner incorrectly asserts that the claimed invention is anticipated by the cited references. Applicants traverse the rejection and respectfully request consideration.

Applicants respectfully submit that the claimed invention is novel over both the Ali and Murphy references. Ali discloses the use of virulent and attenuated viruses to invoke immune response in virus-infected infant rats. Titers were measured in lung and turbinate samples after intranasal infection. The study concluded that titers of virus in the lungs were lower for recombinant viruses than for wild-type viruses, but with considerable overlap. Ali then concluded that infant rats could be used as models to assess virulence of cold-adapted recombinant influenza virus strains.

Murphy discloses the investigation of formalin-inactivated respiratory syncytial virus (RSV) in 4 groups of infants and children (2 groups of vaccinees; 2 groups having had RSV). Serum neutralizing antibody titers were measured as well as antibodies to G and F glycoproteins (by ELISA). Murphy observed enhanced disease in the RSV-infected vaccinees.

In both references, different forms of viruses were used. In Ali, live attenuated viruses were administered. In Murphy, inactivated vaccines were administered. In contrast, the present invention focuses on the use of naked recombinant nucleic acid vaccines. Therefore, the presently claimed invention is not anticipated by the cited art. Accordingly, applicants request the rejection be withdrawn.

III. Rejections under 35 U.S.C. § 103(a)

Claims 1 and 2 stand further rejected as unpatentable over U.S. Patent No. 5,795,872 (to Ricigliano) and Milagres et al. (*Infect Immun* 1994, 62(10):4419-24). The Examiner notes that the claimed invention encompasses delivery of a DNA vaccine and points out that Ricigliano teaches the use of a DNA construct for use in immunization. The Examiner concedes that Ricigliano fails to teach immunization with antigens to specific bacteria species and fails to teach immunization of infants. However, the Examiner incorrectly relies on Milagres for a teaching of a protein *Neisseria meningitidis* vaccine in children. The Examiner alleges that based on the cited references, one skilled in the art would have known to substitute the DNA vectors in place of the protein vaccines. The Examiner also relies on Milagres for a showing of a reasonable expectation of success. Applicants traverse the rejection and respectfully request reconsideration.

Applicants submit that it would not have been obvious for one skilled in the art to substitute DNA vectors in place of the protein vaccines taught in the cited art. First, Milagres discloses a study where a protein vaccine was administered to children of various ages, grouped separately as 3-23 months, 24-47 months, and 48-83 months. Milagres used three assays to measure the antigen/antibody levels of the child populations including antigenic analysis (ELISA), bactericidal antibodies (Ab titers), and immunoblot studies. Milagres concluded that based on the bactericidal data, the functional immune responses were age dependent, that bacterial titers were significantly lower as were bactericidal antibodies in children less than 24 months as compared to the older children. (See page 4422). The remaining test results were deemed not reliable for various reasons.

Applicants submit that the currently pending claims have been amended to further define the target population by amending the claims to read "wherein the infant mammal is immunized within the age of birth to six months" and to further define the vaccine as a "naked recombinant nucleic acid" vaccine. Milagres' conclusion that the functional immune responses are age

dependent make it impossible to know what the results were for children under the age of 3 months or what the breakdown of results were within each group of the study. There is no expectation here that the functional immune response was even present, let alone successful, in the claimed "infant" population. Milagres' conclusions regarding the age dependent nature of the immune response would not create an expectation of success in an infant population as presently claimed.

Secondly, Milagres administered a protein vaccine to conduct his studies. In contrast, the presently claimed invention relates to the administration of naked recombinant nucleic acids encoding a relevant epitope of the target antigen. Reliance on Ricigliano fails to provide one skilled in the art the presently claimed invention. Ricigliano is broadly directed to DNA constructs useful for immunization or gene therapy comprising muscle specific regulatory elements and a DNA sequence. (See col. 4:35-40). According to the Examiner, Ricigliano teaches that any antigen can be inserted into the construct. However, Ricigliano is not enabling for any "antigen", rather Ricigliano requires that the DNA construct contain a muscle specific regulatory element of muscle isozyme of creatine kinase with a specific nucleotide sequence (SEQ ID NO:1; see claim 1). Therefore, neither reference demonstrates the use of nucleic acids specific to relevant epitopes of target antigens as presently claimed. Therefore, it is unlikely that one skilled in the art, based on the cited art, would have reasonably expected that effective immunization of infants from birth to six months could be achieved by administration of a naked recombinant nucleic acid encoding the antigenic peptide. Applicants submit that based on the remarks provided above, the claimed invention is not obvious over the cited art. Accordingly, applicants request that the rejection be withdrawn.

Claims 1 and 2 stand further rejected as unpatentable over Fynan et al. (PNAS 1993, 90(24):11478-82) and Milagres. According to the Examiner, Fynan teaches a variety of specific known antigens for use in DNA constructs for immunization. The Examiner concedes that Fynan fails to teach immunization to a specific antigen or the immunization of infants, but relies on the teaching of Milagres as noted above to arrive at the claimed invention. Because, as explained above, Milagres would produce no reasonable expectation of success in the infant population as presently claimed, it does not supply the deficiencies of Fynan. Accordingly, applicants traverse the rejection and request that it be withdrawn.

IV. Double Patenting

Claims 1 and 2 stand provisionally rejected under 35 U.S.C. § 101 for double patenting over claims 1-47 of co-pending U.S. patent application serial no. 10/351,630. Applicants note that in the event that claims are allowed in either case, appropriate claim cancellations or amendments will be made in the co-pending application to ensure that they are not coextensive in scope.

Since this is a provisional rejection, applicants submit that no such claim amendments are necessary at this time.

V. Conclusion

In view of the above amendments and remarks, it is respectfully requested that the application be reconsidered and that all pending claims be allowed and the case passed to issue. If there are any other issues remaining which the Examiner believes could be resolved through either a Supplemental Response or an Examiner's Amendment, the Examiner is respectfully requested to contact the undersigned at the telephone number indicated below.

Applicants believe that no additional fees are due. If however additional fees are due, the Commissioner is hereby authorized to charge payment of fees or to credit any overpayment associated with this communication to Deposit Account No. 02-4377.

Respectfully submitted,

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